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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,130	11/21/2001	Richard W. Titball	3974-3	1328

7590 01/06/2004

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 01/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,130	TITBALL ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' amendment filed 10-30-03 has been entered. Claims 1-31 have been canceled. Claim 34 has been amended. Claims 32-38 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 32-38 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention and is repeated for the reasons set forth in the preceding Official action mailed 7-30-03 (Paper No. 6). Applicant's arguments filed 10-30-03 have been fully considered but they are not persuasive.

Applicants cite reference "Immunoconjugates in Drug Delivery Systems" and argue that the delivery of the liposomes and immunoconjugates are well known in the art and the specification teaches releasing high concentration of a compound at the tumor site for cancer treatment. Applicants further argue that the present invention is not limited to a specific pharmaceutical agent or disease treatment and the examiner's cited references do not discuss the present invention (amendment, p. 5-6). This is not found persuasive because of the reason set forth in the preceding Official action mailed 7-30-03 (Paper No. 6). A pharmaceutical composition is a composition which implies *in vivo* applicability such that therapeutic effects

against a disease or a disorder are obtained. The claims read on a therapy of using a reconstituted lipase activity by combining two or more lipase components *in vivo* so as to lyse a lipid structure such as liposome and release a pharmaceutical agent, including any small organic molecule, a polynucleotide sequence, a protein, and an antibody, from said lipid structure for the treatment of a particular disease or disorder. The claims encompass using a pharmaceutical composition for gene therapy, protein therapy, immunotherapy and organic compound therapy *in vivo*. Although the method of delivering a pharmaceutical agent to a subject in vivo was known in the art, however, it was unpredictable whether sufficient pharmaceutical composition containing a pharmaceutical agent, such as a small organic molecule, a polynucleotide sequence, a protein, or an antibody, can be delivered via various administration routes so as to provide therapeutic effect for the treatment of a particular disease or disorder *in vivo*. The claims encompass treating any disease or disorder by using any pharmaceutical agent *in vivo*. The specification also fails to provide an adequate guidance for the correlation of the pharmaceutical agent with a specific disease or a disorder such that said pharmaceutical agent could provide therapeutic effects for said specific disease or disorder *in vivo*.

Although the cited references Deonarain, Eck, Verma, and Gorecki are associated with gene therapy in vivo, the rationale is similar for protein and antibody therapy. The delivery route of a protein or an antibody, the amount and stability of the protein or antibody present at the targeted site, and the uptake of the protein or antibody by the targeted cells and its activity within the targeted cells are all important factors for a successful protein therapy or immunotherapy. Further, there is no evidence of record that whether delivery of a first pharmaceutical composition containing an antibody conjugated to a lipase or a lipase component and a second

pharmaceutical composition containing a liposome associated with a lipase component to a targeted site via various administration routes could provide sufficient pharmaceutical agents, including polynucleotides, organic compounds, proteins and antibodies, at the targeted site so as to provide therapeutic effect for a particular disease or disorder *in vivo*.

Applicants argue that the present invention is a two-part drug delivery system including the first part having an antibody conjugated with lipase and a second part having a liposome containing active compound and they are enabled by the specification in examples 1 and 3 (amendment, p. 7-8). This is not found persuasive because of the reason set forth in the preceding Official action mailed 7-30-03 (Paper No. 6) and the reasons set forth above. Example 1 of the present invention only discloses *in vitro* data and *in vitro* data can not be extrapolated to success in delivering pharmaceutical composition to a subject so as to provide therapeutic effect *in vivo*. Example 3 is only a prophetic example of *in vivo* delivery but fails to provide evidence for delivering a pharmaceutical composition to a subject so as to provide therapeutic effect *in vivo*. Thus, the claims remain rejected under 35 U.S.C. 112 first paragraph.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claim 32 remains rejected under 35 U.S.C. 102(b) as being anticipated by Flickinger et al., 1976 (Europ. J. Cancer, Vol. 12, pp. 159-160) and is repeated for the reasons set forth in the

preceding Official action mailed 7-30-03 (Paper No. 6). Applicant's arguments filed 10-30-03 have been fully considered but they are not persuasive.

Applicants argue that claim 32 requires using a lipase from Clostridium perfringes (CPAT), which has ability to lyse liposome, or a modified CPAT which has no or less lipase activity, and the inactive lipase is reconstituted by second lipase component, whereas the cited Flickliger does not teach all of the essential elements of the claim (amendment, p. 8-9). This is not found persuasive because of the reason set forth in the preceding Official action mailed 7-30-03 (Paper No. 6). The claimed pharmaceutical composition comprises an antibody conjugated to a lipase **or** a lipase component, such as N- or C-terminal recombinant CPAT, having no or less lipase activity as compared to lipase holoenzyme and a pharmaceutically acceptable carrier, diluent or excipient. The claimed pharmaceutical composition can read on three components: antibody, lipase and a pharmaceutically acceptable carrier. Flickinger teaches preparation of conjugates of **phospholipase C** to tumor **antibodies** and dialyzed the conjugates against **sterile Earles saline** to ascertain the cytotoxic effect upon the homologous tumor cells (e.g. p. 159). The Earles saline is considered a pharmaceutically acceptable carrier, diluent or excipient. Thus, claim 32 is anticipated by Flickinger.

Conclusion

No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. Due to the move of USPTO to new site in Alexandria, Virginia, examiner's telephone number will be changed to (571) 272-0726 **after January 12, 2004**. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

S. Chen

Shin-Lin Chen, Ph.D.